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Retinal Alterations Detected Using Optical Coherence Tomography in Children with Strabismus

Şaşılığı Olan Çocuklarda Optik Koherens Tomografi ile Tespit Edilen Retinal Değişiklikler

Retinal Alterations in Strabismus

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Özet

Bu çalışmanın amacı şaşılık hastaları ile normal olguların retina sinir lifi tabakası (RSLT) ve fovea kalınlıklarını karşılaştırmayı ve ambliyopinin sonuçlara etkisini araştırmak idi. Katılımcılar dört gruba ayrıldı. Grup 1'e şaşılığı olup ambliyopisi olmayan hastaların her iki gözü (40 göz) dahil edildi. Şaşılık ambliyopisi olan hastaların gözleri, ambliyopik gözleri (Grup 2'de 21 göz) ve diğer gözleri (Grup 3'de 21 göz) olarak iki gruba ayrıldı. Grup 4 kontrollerin her iki gözleri (40 göz) dahil edilerek oluşturuldu. Üst ve alt kadranlardaki ortalama RSLT kalınlığı Grup 2 ve Grup 3'de Grup 4'e göre daha ince bulundu (p<0.05). Ayrıca, nazal kadran makula kalınlığı Grup 3'de Grup 1'den daha yüksek bulundu (p=0.041). Alt kadran makula kalınlığı Grup 2'de Grup 1'e göre daha kalın bulundu (p=0.043). Fovea merkezi ve makula temporali kalınlığı Grup 3'de Grup 4'e göre daha kalındı (sırasıyla p=0.04, p=0.005). Bu çalışmada ambliyopisi olan ve olmayan şaşılık hastalarında retinada yapısal değişiklikler gözlemlendi. Bu retinal değişiklikler daha önceki çalışmalarda bildirildiği gibi ambliyopide görülen lateral genikulat cisimdeki değişliklerin sonucu olabilir. Bu hipotezi açıklamak için daha geniş vaka serileri gerekmektedir.

Anahtar Kelimeler

Ambliyopi; Şaşılık; Optik Koherens Tomografi

Abstract

The aim of this study was to compare the thickness of the retinal nerve fiber layer (RNFL) and fovea of strabismus cases with normal cases and assess the effect of amblyopia on the results. The partipicians were divided into four groups. Group 1 included both eyes (40 eyes) of strabismus patients without amblyopia. Patients eyes, who had stabismic amblyopia, divided in two group as amblyopic eyes (21 eyes in Group 2) and the other eyes (21 eyes in Group 3). Group 4 enclosed both eyes (40 eyes) of the controls. The thickness of the RNFL across the superior quadrant in Group 1 was thinner with respect to that of the control group (Group 4) (p<0.05). The mean thickness of the RNFL across the superior and inferior quadrants in Group 2 and Group 3 was thinner in comparison to Group 4 (p<0.05). Moreover, the macular thickness in the nasal quadrant was thicker in Group 3 than Group 1 (p=0.041). The macular thickness in the inferior quadrant was thicker in Group 2 than Group 1 (p=0.043). The thickness of the fovea center and macular temporal quadrant in Group 3 was thicker than Group 4 (p=0.04, p=0.005, respectively). In this study, that was observed the structural changes in the retina of the strabismus patients with and without amblyopia. These retinal alterations may be result of structural changes in lateral geniculate body in cases with amblyopia which has been reported in previous studies. Larger case series are needed to clarify this hypothesis.

Keywords

Amblyopia; Strabismus; Optical Coherence Tomography

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Introduction

Strabismus is a visual disorder in which the axes of the eyes become unparallel. Strabismus can be monitored constantly in one eye or intermittently between two eyes. The presence of strabismus in one eye creates a serious risk for the development of amblyopia. Animal studies have demonstrated that the development of blurred vision and strabismus causes structural and functional damages in the lateral geniculate nucleus (LGN) and striated cortex.[1]

Optical coherence tomography (OCT) is a noninvasive technique providing in vivo sectional images of the retina with high resolution. The OCT has been used because of these features in order to investigate retinal changes in amblyopia. However, the studies evaluating the structural changes in the retina of strabismus patients with OCT are limited in literature. Therefore, in the present study we aimed the comparison of RNFL and macular thickness of strabismic children with healthy children and assessed the alteration of these results in the presence of amblyopia.

Material and Method

The strabismic patients with or without amblyopia were included to the study group. The patients were divided into three groups and a control group was also included from healthy children with the same age. The patients with nystagmus, incomitant strabismus0, eccentric fixation, ophthalmologic problems leading poor vision, spherical or cylindrical refractive errors in both eyes with > ± 5 diopter (D) in patient group and > ± 1D in control group were excluded from the study. According to determined criteria we formed four groups. Group 1 contained 40 eyes of the strabismic children with no amblyopia, Group 2 consisted of 21 amblyopic eyes of the patients with strabismus and amblyopia, Group 3 included 21 healthy eyes of patients with strabismus and amblyopia, and finally the 4th Group was the control group consisting of 40 eyes of healthy children. Corrected and uncorrected visual acuities were measured using Snellen level and cycloplegic refraction measurements were recorded. Prism cover test was used to measure the amount of near and far squint in strabismic cases. Moreover, Spectral Domain OCT/ SLO (Opko/OTI, Inc., Miami, FL) was used for the measurements of all the cases after the generation of cycloplegic mydriasis. Fast RNFL protocol was used to analyze the thickness of the RNFL. Mean RNFL and the thickness of the RNFL across the superior, inferior, nasal, and temporal quadrants were recorded. Macular thickness was determined by the ETDRS circle with 6mm in diameter in nine regions. Whole the measurements of SDOCT were performed by an independent person from the present study.

SPSS 18.0 Package Program was used for statistical analysis. The comparison of the measurements between the groups were performed by using chi-square test. General comparisons of numerical measurements pertaining to the groups were realized by Kruskal–Wallis test and One-way ANOVA tests. Scheffe, Tamhane tests, and Mann Whitney U test were used for the paired subgroup analysis.

Results

The mean age of the patients in Group1 was 12± 3.7 (6-18), 11± 3.6 (6-18) in Groups 2 & 3, and 11.4 ± 3.3 (5-18) in Group 4. There was no significant difference between the mean ages of the groups statistically. Demographic features of the cases are illustrated in Table 1. All strabismic patients have mild to moderate esotropia. The mean squint amount was 18 prism diopter (range; 8-22 prism diopter).

We found that the mean RNFL values were 100.38μm in Group 1, 94.38μm in Group 2, 97.48μm in Group 3, and 109.08μm in Group 4. The thickness of the RNFL across the optic disc, superior, and inferior quadrants and the mean thickness of the RNFL were markedly increased in Group 4 (the control group) with regard to Groups 1, 2, and 3. However, we noted no considerable difference between the superior and inferior quadrants of Group 1 in comparison to Group 2 and Group 3 (Table 2).

Moreover, we inspected fovea center, the superior, inferior, nasal, and temporal quadrants for the analysis of the macular thickness. Mean macular thickness across the fovea center was 99.43μm in Group 1, 115.86μm in Group 2, 124.33μm in Group 3, and 96.4μm in Group 4. No marked variation was observed at the thickness of fovea center, temporal, and nasal macula among the groups. Similarly, we noticed no significant difference in the thickness of superior and inferior quadrants among the groups. The results of the analysis are summarized in Table 3.

Discussion

Abnormal position of the visual axis in strabismus causes diplopia and visual confusion.[2] Some adaptive mechanisms develop in time to remove or minimize these effects. The change of foveal fixation from one eye to the other eye in alternating strabismus is one of the adaptive mechanisms; thereby, both eyes sequentially take over the fixation. In the other mechanism, one of the eyes becomes dominant and tries to inhibit visual confu-

Table 1. Demographic features of the patient groups.

	Group 1	Group 2 and 3	Group 4	p value
Age (Year)	11,9 ± 3,7	10,8 ± 3,6	11,4 ± 3,3	> 0,05
Gender n (%)				
Male	6 (30)	14 (70)	8 (38)	
Female	13 (61)	8 (40)	12 (60)	> 0,05

Table 2. Retinal nerve fiber layer (RNFL) thickness values in the groups

RNFL thickness	Group 1	Group 2	Group 3	Group 4	p value (μm)
Temporal	72,28 ± 12, 79	66,43 ± 20,68	71,9 ± 20	74,12 ± 10,48	> 0,05
Superior	122,43 ± 19,76	112,86 ± 33,58	117,57 ± 20,87	137,45 ± 19,54	0,01
Nasal	80, 65 ± 14,72	88,19 ± 31	83,43 ± 26,64	89,43 ± 18,3	0,05
Inferior	125,1 ± 20,97	111,05 ± 30,26	118,48 ± 23,78	137,28 ± 15,95	0,01
Mean RNFL thickness	100,38 ± 12,31	94,38 ± 21,13	97,48 ± 15,57	109,08 ± 10,36	0,02

Table 3. Macular thickness values.

Macular thickness	Group 1	Group 2	Group 3	Group 4	p value (μm)
Temporal	198,4 ± 66,4	222 ± 56,18	229,9 ± 58,42	168,82 ± 62,28	0,04
Superior	226,28 ± 65,96	230,76 ± 52,72	251,52 ± 62,2	216,95 ± 61	0,097
Nasal	208,25 ± 77,47	241,57 ± 47,11	256,29 ± 52	211,25 ± 52,25	0,014
Inferior	211,43 ± 72,74	258,29 ± 35,76	243,71 ± 61,63	229,5 ± 54,61	0,051
Central fovea	99,43 ± 34,29	115,86 ± 39,5	124,33 ± 46,67	96,4 ± 35,97	0,029

sion arising from the other eye. The latter mechanism causes strabismic amblyopia in nondominant eye. Several experimental studies show that the number of neuronal activities in visual cortex decrease in strabismic amblyopia.[3,4] Moreover, studies also demonstrate that the occurrence of strabismus and visual confusion during the early visual development stage yields to structural and functional damages in the LGN and striated cortex.[5-7]

In order to measure the thickness of the RNFL in vivo, optical coherence tomography (OCT) have been used in various ophthalmological diseases, particularly for the investigation of the association between amblyopia and retinal nerve fiber thickness. Bozkurt et al. examined eighteen anisometropic, two strabismic, and four combined amblyopia cases with a mean age of 28-years.[8] Caramelli et al. inspected 21 patients with strabismic amblyopia. These studies did not reported statistically meaningful difference in iNFA-GDx parameters between normal and amblyopic eyes.[9] In respect to these data, we compared retinal nerve fiber thickness of strabismus patients with or without amblyopia with healthy children. We attempted to determine the value of OCT as an early identification method in the diagnoses of strabismic amblyopia through assessing the changes in RNFL in strabismus.

In order to form a nomogram and compare the examined eye with the healthy eye fixed screening diameter is required. Schuman et al. proposed the use of 3mm and 4mm- screening diameter, which is accepted in general.[10] In the present study we used this fixed screening circle. The setback with the use of fixed screening circle is the obtainment of the measurements over larger areas in hypermetropic persons; thereby, optic nerve head is measured thicker in hypermetropic cases and thinner in normal individuals. Therefore, the patients with high hypermetropia and high myopia were excluded from the current study.

Huyn et al. reported the mean thickness of RNFL in 6-years old children as 103.7 μm.[11] Likewise, Sony et al. also reported the mean thickness of RNFL as 104.27μm in healthy individuals and the decrease in the thickness of RNFL with age was statistically significant.[12] Besides, Budenz et al. examined the association between axial length & refraction error and the thickness of RNFL and demonstrated that 1 mm increase in the axial length increased RNFL thickness by 2.2 μm and 1 diopter change in refraction error towards myopia reduced RNFL thickness by 0.9 μm.[13] In the present study, the effect of age on the thickness of RNFL was not considered because age differences did not exist between the groups.

Furthermore, Yoon et al. found that peripapillary RNFL was markedly thick in anisometropic amblyopia cases.[14] Some studies reported that while the thickness of RNFL in strabismic amblyopia was not different from the controls, its thickness was notably increased in refractive amblyopia with respect to controls.[15,16] Nevertheless, there are some studies showing that no difference was present in the thickness of RNFL between normal eyes and amblyopic eyes regardless of the type of amblyopia.[17,18]

Localized alterations are suggested to initiate in central nervous system or retina after visual deprivation in strabismic amblyopia. Consequently, structural and functional changes occur in visual cortex, LGN, and ganglion cells pertaining to amblyopic eye. The number and size of the axons of ganglion cells decrease, and this decrease is considered to result with the reduction in the thickness of RNFL. This theory can explain the decrease across the superior quadrant in strabismic eyes, in the mean thickness of RNFL, and decline across superior and inferior quadrants in amblyopia in the current study. Repka et al. demonstrated that the thickness of RNFL in strabismic amblyopia was about 5μm thinner than the amblyopic eye even though it was not statistically significant.[19]

In the literature, there is only one study examining the thickness of RNFL in strabismus cases without amblyopia. Reche-Sainz et al. studied the thickness of RNFL in esotropia and exotropia cases and compared the results with the controls, and reported no statistically significant difference between them. [20] In the present study we noted marked reduction in the thickness of RNFL across the superior quadrant in strabismic cases.

Even though it was not statistically significant Huynh et al. reported that the thickness of macular center in amblyopic eyes was slightly thicker than the normal eyes.[18] In contrast to the studies showing an increase in the macular thickness in strabismic amblyopia with respect to controls, there are some studies indicating no difference in the macular thickness in strabismic amblyopia with regard to healthy cases.[16,21,22] In this study, we noted no statistically meaningful variation in the thickness of the strabismic amblyopic eyes across their nasal and superior quadrants, and their mean macular thicknesses in comparison with other study groups. In the strabismic amblyopic eyes the thickness of temporal quadrant was found to be thicker than the control group wheras inferior quadrant was thicker than the strabismic cases. Likewise, although it was not meaningful, the thickness of macular center was augmented in amblyopic eyes in comparison to the controls. Increased macular thickness in the strabismic amblyopic eyes is argued to be owing to incomplete developmental stage, particularly the inhibition of foveal depression. The changes in the thickness of macula could be explained with the theory stating that differential neuronal looses can occur at various extents depending on the etiology of amblyopia.

We did not encounter studies examining the macular thickness in strabismus patients without amblyopia in the literature. In the present study, we measured the thickness of macula in strabismus patients without amblyopia and noted no marked difference in comparison with the controls. We propose that the increase in the thickness of macula in strabismic amblyopia could yield to both the presence of notably thinner inferior quadrant in strabismic eyes than strabismic amblyopic eyes and the occurrence of markedly thinner nasal quadrant in strabismic eyes than healthy eyes of strabismic amblyopic patients.

Certain parameters of RNFL measurement determined by using OCT in strabismic eyes were different than those of control group. Although several studies demonstrate the existence of damage in upper visual pathways (LGN and visual cortex), in amblyopia, the observation of changes in macula and RNFL indicate that pathological alterations also occur at retinal level. [23,24] Detection of markedly thin RNFL and gradually increased macular thickness determined at various OCT measurements can be a warning for the development of amblyopia. We also observed thinner nasal measurements in cases with strabismus in regard to healthy eyes of cases with strabismic amblyopia.

In conclusion, histological studies are needed to demonstrate the presence of retinal damage in amblyopia. However, with the present study we are hopefull for the use of optical coherence tomography as an early identification tool in the diagnosis of amblyopia in strabismus cases.

Competing interests

The authors declare that they have no competing interests.

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